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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,828	12/22/2005	Jeffrey B. Stock	18016-20	2870
530 7590 09/02/2009 LERNER, DAVID, LITTENBERG, KRUMHOLZ & MENTLIK 600 SOUTH AVENUE WEST WESTFIELD, NJ 07090				
EXAMINER YANG, NELSON C				
ART UNIT		PAPER NUMBER		
1641				
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09/02/2009		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/561,828

**Applicant(s)**

STOCK, JEFFRY B.

**Examiner**

Nelson Yang

**Art Unit**

1641

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 June 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 2-7, 9, 10, 28, 29, 32, 35, 54, 58 and 63-73 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-7, 9, 10, 28, 29, 32, 35, 54, 58 and 63-73 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 December 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Election/Restrictions***

1. Applicant's election without traverse of claims 63, 2-7, 9-10, 28-29, 32, 35, 54, 58, 64-73 in the reply filed on June 12, 2009 is acknowledged.

***Response to Amendment***

2. Applicant's amendment of claims 2-6, 9, 10, 28-29, 32, 35, 54, 58, 64-66, 73 is acknowledged and has been entered.
3. Applicant's cancellation of claim 1 is acknowledged and has been entered.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 64 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 64 recites the limitation "the surface" in the claim. There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1641

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 63, 2-7, 9, 10, 28, 29, 32, 35, 54, 66, 68-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blau et al. [US 2002/0048778] in view of Williams [Williams et al., Functional similarities among two-component sensors and methyl-accepting chemotaxis proteins suggest a role for linker region amphipathic helices in transmembrane signal transduction, 1999, Molecular Microbiology, 33(6): pp.1093-1102].

8. In particular, with respect to claim 63, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF along with phycoerythrin labeled antibodies (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer, which allows for the monitoring and quantitation of interactions in the cell (see entire patent). Blau et al., however, do not teach the use of methyl-accepting chemosensory receptors or a portion thereof.

Williams et al., however, teach that two-component sensors and methyl-accepting chemotaxis proteins modulate specific phosphoryl relay systems that couple environmental signals to appropriate cellular responses (p.1093, col.1-2). Williams et al. further teach that the sensors are able to detect periplasmic signal binding with subsequent conformational changes being transduced by transmembrane signal transduction (p. 1093, col.1), and are capable of response to, or modulation by different analytes such as ArcB, FixL<sub>Rms</sub>, KdpD, and VirA<sub>At</sub> (p.1094, col.2).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have substituted the sensors and methyl-accepting chemotaxis proteins of Williams in the device of Blau et al. to detect interaction in living cells such as E.coli that are based on environmental signals that modulate signal transduction such as protein-kinase activities.

9. With respect to claim 2, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). Thus the fluorescein and rhodamine bind indirectly to targets via the EGF receptor (para. 0046).

10. With respect to claim 3, Williams et al. teach different two-component histidine kinases may be used with the methyl-accepting chemotaxis proteins (p. 1093, col.1-2, 1094, col.1-2).

11. With respect to claim 4, Williams et al. teach that the signal transduction is ligand responsive and causes a conformational change within the cytoplasmic output domain, shifting it into its alternative signaling state (p.1094, fig.1)

12. With respect to claim 5, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186). The fluorescein and rhodamine labeled EGF would not be naturally occurring entities.

13. With respect to claims 6-7, Blau et al. teach that the invention allows for the monitoring and quantitation of interactions (para. 0070). Williams et al. further teach that the sensors

embody the modulated kinase activity (p. 1093, col.1), and are capable of response to, or modulation by different analytes such as ArcB, FixL<sub>Rm</sub>, KdpD, and VirA<sub>At</sub> (p.1094, col.2).

14. With respect to claims 9, 29, Blau et al. teach in vitro selection (para. 0159).

15. With respect to claims 10, 66, Williams et al. teach sensory moieties comprising four-helix bundle receptor protein binding domains which are separate from the methyl-accepting chemotaxis proteins, which would include the cytoplasmic domain (p.1094, fig. 1).

16. With respect to claim 28, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF along with monoclonal and phycoerythrin labeled antibodies (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186).

17. With respect to claim 32, Williams et al. teach sensory moieties comprising four-helix bundle receptor protein binding domains (p.1094, fig. 1).

18. With respect to claims 35, 65-66, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186), and may be used in cells such as E. coli (para. 0068), which is a chemosensory cell and would comprise methyl-accepting chemosensory receptors.

19. With respect to claims 54, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling

moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186),

20. With respect to claims 68-72, Blau et al. teach an invention for detection of interaction in living cells (abstract) comprising fluorescein and rhodamine labeled EGF (sensing and signaling moieties) is added to cells for in order to detect interaction of fluorescently-labeled molecules within a cell or cell membrane using fluorescence energy transfer (para. 0186), and may be used in particular in cells such as E. coli (para. 0068) which is a chemosensory cell that comprises methyl-accepting chemosensory receptors. The fluorescein and rhodamine labeled EGF would not be naturally occurring entities. Blau et al. further teach that the invention allows for the monitoring and quantitation of interactions (para. 0070).

21. Claims 58 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blau et al. [US 2002/0048778] in view of Williams [Williams et al., Functional similarities among two-component sensors and methyl-accepting chemotaxis proteins suggest a role for linker region amphipathic helices in transmembrane signal transduction, 1999, Molecular Microbiology, 33(6): pp.1093-1102] as applied to claim 63 above, and further in view of Kelso [US 2003/0129296].

With respect to claim 58, Blau et al. and Wun et al. teach fluorescent labels, but fail to teach FRET labels.

Kelso, however, teaches that labels may comprise quantum dots (which are semiconductor nanocrystals) (para. 0072) as well as energy transfer conjugates (para. 0078), which may be used in FRET assays. Kelso thus shows that semiconductor nanocrystals and energy transfer conjugates are equivalent structures known in the art.

Therefore, because these two were art-recognized equivalents at the time the invention was made, one of ordinary skill in the art would have found it obvious to substitute FRET conjugate labels for semiconductor nanocrystals in the sensor of Daniels et al.

***Response to Arguments***

22. Applicant's argument with respect to the title is acknowledged and corrections to the title are currently being addressed.
23. Applicant's arguments with respect to claims 63, 2-7, 9-10, 28-29, 32, 35, 54, 58, 64-73 have been considered but are moot in view of the new ground(s) of rejection.

***Conclusion***

24. No claims are allowed.
25. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.



26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571)272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571)272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

27. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nelson Yang/  
Primary Examiner, Art Unit 1641